REMARKS

Prior to amendment, Claims 1-3 were present in the application and stand rejected. By the forEgoing amendments, Claim 1 has been modified to require that the composition comprises from 1 mM to 250 mM of ethylenediaminetetraacetic acid (EDTA), from 5 mM to 250 mM of Tris (hydroxymethyl) aminomethane, a pharmaceutically acceptable antibiotic or antifungal and a pharmaceutically acceptable carrier. Support for these amendments is found in the specification at page 7, line 6, through page 8, line 4; page 20, line 17, through page 21, line 6; and elsewhere in the application as filed. New Claims 4 and 5 have been added to provide that the antibiotic or antifungal in the composition is selected from preferred groups of antibiotics and antifungals. Support for these new claims is found in the specification at page 8, line 20, through page 9, line 9; page 20, line 17, through page 21, line 6; and elsewhere in the application as filed. It is believed that Claims 1-5 are in condition for allowance in view of the foregoing amendments and following comments. Reconsideration and favorable action is requested.

Rejection of Claims 1-3 under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1-3 under 35 U.S.C. 102(b) as being anticipated by Holly et al. (US 5,380,303). According to the Examiner, Holly et al. teaches the use of an antimicrobial agent in combination with a chelating agent such as EDTA and a buffer in an ophthalmic composition (citing the abstract and claim 1). The Examiner indicated that the claimed combination has been previously used in an ophthalmic formulation and the antimicrobial activity of the claimed composition is taught in Holly et al. Finally, the Examiner indicated that the determination of microbial population and the effective treatment (Claim 2) is considered to be within the skill of the medical professionals, and to store a pharmaceutical composition in some type of kit or container (Claim 3) is the inherent property of any pharmaceutical formulation.

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The Holly et al. '303 patent relates specifically to the use of a known industrial polymeric antimicrobial agent, poly[oxyethylene(dimethylimino)-ethylene-(dimethylimino)ethylene dichloride] in a pharmaceutical preparation in combination with a buffer and metal ion chelating agent for application to ophthalmic solutions for disinfecting contact lenses and preserving ocular solutions used to treat contact lenses and ocular disease (see column 4, lines 48-55). The Holly et al. '303 patent teaches directly away from using small molecule antibiotics and antifungals in the disclosed composition. As disclosed in the Holly et al. '303 patent at Column 2, lines 35-47:

> The monomeric antibacterial agents listed earlier ["Polyquad" or alpha-4[1-tris(2-hydroxyethyl) ammonium chloride-2-dibutenyl] poly[1-dimethyl ammonium chloride-2-dibutenyl]-.omega.-tris (2-hydroxyethyl) ammonium chloride, and "Dymed" or poly[aminopropyl-bis(biguanide)] or poly[hexamethylene-bis(biguanide)]] cannot be added to ophthalmic formulations likely to be used by patients who wear hydrogel contact lenses because the small molecular size of these agents enable them to penetrate pores of hydrogels, the polymeric matrices of the hydrogel materials. The antimicrobial agent accumulated within the lens matrix would eventually leach into the tear film upon application of the lens to the eye. The pore size in poly(hydroxyethylmethacrylate) [poly(HEMA)] gels used in the fabrication of hydrogel lenses is approximately 30-50 Angstroms, as reported in Hydrogels in Medicine and Pharmacy, Vol. II, Polymers. Ed. Peppas, N. K., CRC Press, Inc.

Accordingly, the Holly et al. '303 patent teaches away from the use of small molecule antibiotics or antifungals in its ophthalmic solutions, and specifically does not disclose or remotely suggest inhibiting a microbial infection of an eye by contacting an eye of a patient with a composition comprising from 1 mM to 250 mM of ethylenediaminetetraacetic acid (EDTA), from 5 mM to 250 mM of Tris (hydroxymethyl) aminomethane, a pharmaceutically acceptable antibiotic or antifungal and a pharmaceutically acceptable carrier, as claimed in applicants' amended claims.

As disclosed in the present application, the antibiotics and antifungals of applicants' compositions have increased antimicrobial activity because of the synergy with the chelating

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agent (EDTA) and maintenance of the treated area at a pH suitable for sustained antibiotic or antifungal activity. The antibiotic or antifungal agent can, therefore, be used in effective doses that are less than would be required for the same level of antimicrobial activity in the absence of the chelator. See, for example, the specification at page 2, lines 17-23, and the Examples. Accordingly, the therapeutic compositions of the invention are ideally suitable for administering to the surface of an eye for the repair or healing of a wound to the conjunctiva or corneal surface.

Since the Holly et al. '303 patent does not teach or remotely suggest inhibiting a microbial infection of an eye by contacting the eye with a composition comprising from 1 mM to 250 mM of ethylenediaminetetraacetic acid (EDTA), from 5 mM to 250 mM of Tris (hydroxymethyl) aminomethane, a pharmaceutically acceptable antibiotic or antifungal and a pharmaceutically acceptable carrier, it cannot anticipate applicants' Claims 1-3 under 35 U.S.C. § 102(b). In addition, since the Holly et al. '303 patent teaches the alleged advantages of polymeric poly[oxyethylene(dimethylimino)-ethylene-(dimethylimino)ethylene dichloride] as an ophthalmic antimicrobial and teaches away from the use of conventional antibiotics and antifungals, the invention of applicants' amended claims would not have been obvious to a person of ordinary skill in the art under 35 U.S.C. § 103 in view of this reference. Accordingly, the Examiner's rejection of claims under 35 U.S.C. § 102(b) should properly be withdrawn.

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CONCLUSION

In view of the foregoing amendments and comments, it is believed that Claims 1-5 are in condition for allowance. Entry of the claim amendments, reconsideration, and favorable action are requested. The Examiner is further requested to contact the applicants' undersigned representative to discuss any issues that may facilitate prosecution of the application.

Respectfully submitted,

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